

JC12 Rec'd PCT/PTC 21 APR 2005

CLAIMS.

A technetium complex composition which comprises a metal complex of the 1. radioisotope *Tc with a ligand of Formula (I):

where: 10

each R¹ and R² is independently an R group;

x is 94m, 99 or 99m;

Y is $-(A)_n-Z$

where: Z is a biological targeting moiety of molecular weight less than 5,000;

-(A)_n- is a linker group where each A is independently -CO- , -CR₂- , -CR=CR- , -C \equiv C- , -CR₂CO₂- , -CO₂CR₂- , -NR--NRCO-, -CONR-, -NR(C=O)NR-, -NR(C=S)NR-, -SO₂NR-, -NRSO₂-, -CR₂OCR₂-, -CR₂SCR₂-, -CR₂NRCR₂-, a C₄₋₈ cycloheteroalkylene group, a C₄₋₈ cycloalkylene group, a C₅₋₁₂ arylene group, or a C₃₋₁₂ heteroarylene group or a polyalkyleneglycol, polylactic acid or polyglycolic acid moiety; n is an integer of value 0 to 10;

each R group is independently H or C₁₋₁₀ alkyl, C₃₋₁₀ alkylaryl, C₂₋₁₀ alkoxyalkyl, C₁₋₁₀ hydroxyalkyl, C₁₋₁₀ fluoroalkyl, or 2 or more R groups, together with the atoms to which they are attached form a carbocyclic, heterocyclic, saturated or unsaturated ring;

wherein:

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- (i) less than 10 % of the *Tc present in the technetium complex composition comprises transient *Tc complexes of the ligand of Formula I; and
- (ii) less than 5 % of the *Tc present in the technetium complex composition comprises lipophilic *Tc complexes of the ligand of Formula I.
- 2. The technetium complex composition of claim 1, wherein less than 5 % of the

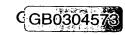
 *Tc present in the technetium complex composition comprises transient *Tc
 complexes of the ligand of Formula I.
- 3. The technetium complex composition of claims 1 or 2, wherein less than 3 % of the *Tc present in the technetium complex composition comprises lipophilic *Tc complexes of the ligand of Formula I.
- 4. The technetium complex composition of claims 1 to 3, where x is 99m.
- 5. The technetium complex composition of claims 1 to 4, where Z is a peptide of 3 to 20 amino acids.
- 6. The technetium complex composition of claim 5, wherein the peptide of 3 to 20 amino acids is a fragment of ∞ -antiplasmin.
- 7. The technetium complex composition of claim 6, wherein the fragment of ∞2 25 antiplasmin comprises the tetrapeptide Asn-Gln-Glu-Gln.
 - 8. The technetium complex composition of claim 7, wherein the fragment of ∞ antiplasmin comprises the peptide:

Asn-Gln-Glu-Gln-Val-Ser-Pro-Xaa-Thr-Leu-Leu-Lys-Gly, where Xaa is Tyr or I-Tyr.

9. The technetium complex composition of claims 1 to 8, wherein Y is -CH₂CH₂-NR-(A)_m-Z, where m is an integer of value 0 to 5.



10 mg 2 mg



- 10. The technetium complex composition of claims 1 to 9, where each R¹ is independently C₁₋₃ alkyl, C₂₋₄ alkoxyalkyl, C₁₋₃ hydroxyalkyl, or C₁₋₃ fluoroalkyl.
- 5 11. The technetium complex composition of claims 1 to 10, where the ligand is of Formula (II):

where: each R^1 is independently C_{1-3} alkyl or C_{1-3} fluoroalkyl; and p is an integer of value 0 to 3.

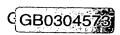
- 12. The technetium complex composition of claim 11, where (A)_p is -CO- or NR-.
- 15 13. The technetium complex composition of claims 11 and 12, where each R¹ is CH₃ and (A)_p is NH and Z is Ac-Asn-Gln-Glu-Gln-Val-Ser-Pro-Xaa-Thr-Leu-Leu-Lys-Gly-, where Xaa is Tyr or I-Tyr, and Ac is N-acetyl.
- 14. The technetium complex composition of claims 1 to 13, which further comprises a radioprotectant.
 - The technetium complex composition of claim 14, where the radioprotectant is para-aminobenzoic acid or a biocompatible salt thereof.
- 25 16. A radiopharmaceutical which comprises the technetium complex composition of claims 1 to 15 in a form suitable for mammalian administration.
 - 17. The radiopharmaceutical of Claim 16, where *Tc is ^{99m}Tc.

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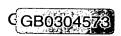
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- 18. A kit for the preparation of the technetium radiopharmaceutical of claims 16 or 17, which comprises:
 - (i) the ligand of Formula (I) of claim 1;
 - (ii) a biocompatible reducing agent,
 - (iii) a weak organic acid or a salt thereof with a biocompatible cation.
- 19. The kit of claim 18, wherein the ligand is as defined in Claims 5 to 10.
- 20. The kit of claim 19, where the ligand is of Formula II as defined in claims 11 to 13.
- 21. The kit of claims 18 to 20, which further comprises a pH-adjusting agent.
- 22. The kit of claims 18 to 21, wherein the biocompatible reducing agent comprises stannous.
- The kit of claims 18 to 22, wherein the weak organic acid is acetic acid, citric
 acid, tartaric acid, gluconic acid, glucoheptonic acid, benzoic acid, a phenol or a phosphonic acid.
 - 24. The kit of claims 18 to 23, which further comprises a radioprotectant.
- 25. The kit of claim 24, wherein the radioprotectant comprises *para*-aminobenzoic acid or a biocompatible salt thereof.
 - 26. The kit of claims 18 to 25, which is lyophilised.

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- 27. The kit of claims 18 to 26, which comprises:
 - (i) the ligand of Formula II of claim 13;
 - (ii) a biocompatible reducing agent which comprises stannous;
 - (iii) a weak organic acid or salt thereof with a biocompatible cation which comprises methylenediphosphonic acid;
 - (iv) a radioprotectant which comprises para-aminobenzoic acid or a biocompatible salt thereof;
 - (v) a pH-adjusting agent which comprises sodium bicarbonate.

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28. A method of diagnostic imaging of thrombi using the radiopharmaceutical of claim 16, wherein the technetium complex composition is as defined in claims 6 to 8.

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